REMARKS

Initially, the Examiner is respectfully requested to return an initialed copy of the Form PTO/SB/08 filed with Applicants' Disclosure Statement of December 19, 2005.

Claims 1-9 and 24 are pending.

At page 5 of the Action, claims 1, 2, [7,] 8, 9 and 24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 7,034,153 (Nakai et al.).

This rejection should be withdrawn because the present claims are not obvious over claims 1 and 2 of Nakai et al.

The Examiner asserts that although the conflicting claims are not identical, they are not patentably distinct from each other.

The Examiner considers that in Nakai et al.,

1) 8-(3-Pentylamino)-2-methyl-3-(2-chloro-4-methoxyphenyl)-6,7-dihydro-5H-cyclopenta[d]pyrazolo[1,5-a]pyrimidine (to be referred as "compound A" hereinafter) and a pharmaceutically acceptable salt thereof is disclosed (page 5, lines 14-16 of the Office Action);

2) the hydrochloride salt is taught (page 5, line 16 of the Office Action);

3) the methanesulfonate salt is taught (page 5, lines 16-17 of the Office Action); and

4) the intended uses are taught (page 5, lines 17-18 of the Office Action).

Additionally, the Examiner states that

5) it is routine experimentation to make a methanesulfonate salt of an amine compound and if the compound A is obvious, methanesulfonate salt thereof is obvious (page 5, lines 18-20 of the Office Action);

6) if the crystalline form of any compound is introduced into a pharmaceutically acceptable carrier, which is a liquid, the crystallinity of the compound is lost (page 6, lines 1-3 of the Office Action); and

7) with regard to the arguments submitted on February 25, 2009 as a response to the Office Action, the Examiner asserts that the arguments are not persuasive and thermal stability of methanesulfonate salt of the compound A is not unexpected. Specifically, the Examiner cites Bastin et al. and states that it is known in the art that mesylate salts have high melting points. Furthermore, the Examiner cites Berge et al., and states that the publication discloses the mesylate salt as one of the most popular anionic salts which is FDA approved commercially. The Examiner considers that one of ordinary skill in the art would make mesylate salt based on Berge et al. and expect a higher melting point salt compound (from page 6, line 4 to page 7, line 5 of the Office Action).

Applicants respectfully disagree.

At page 427, left column, lines 8-14 (abstract), Bastin et al. discloses that "the salt form selected will influence a range of other properties such as melting point, hygroscopicity, chemical stability, dissolution rate, solution pH, crystal form, and mechanical properties. Where possible, a range of salts should be prepared for each new substance and their properties compared during a suitable preformulation program." Therefore, contrary to the Examiner's assertion, Bastin et al. acknowledges that selection of a suitable salt for each compound is an unpredictable process.

Additionally, although Bastin et al. discloses that mesylate salt of the compound RPR 127963 has a higher melting point than that of the hydrochloride of the compound (Table 5 at page 432), the mesylate salt of RPR 111423 disclosed in Table 4 at page 431 and the mesylate

salt of RPR 200765 disclosed in Table 7 at page 433 show lower melting points than those of the hydrochlorides of the respective compounds. Therefore, mesylate salts do not necessarily show superior thermal stability and suitable salts of each compound must be determined by experimentation.

Furthermore, in WO 03/049688 (page 4, line 11 to page 7, line 4), a copy of which is submitted herewith, acid addition salts such as mono- and bis-hydrochlorides, mono- and bis-methanesulfonates, mono-maleates and mono-phosphates are evaluated. It is disclosed that salts other than bis-hydrochloride monohydrates are not suitable for medicaments because of their physical instability. Additionally, in WO 99/36404 (page 3, lines 6-23), a copy of which is submitted herewith, acid addition salts such as the hydrochloride, benzenesulfonate, methanesulfonate, p-toluenesulfonate, phosphate, nitrate, 1,2-ethanedisulfonate, isethionate, sulfate and bisulfate salt of HIV protease inhibitor are evaluated and it is disclosed that the bisulfate salt has the best solubility of them all. That is, the above two WO publications indicate that even if Berge et al. was considered, one skilled in the art would not have been motivated to makethe methanesulfonate salt and the thermal stability thereof would not have been expected.

In view of the above, Applicants respectfully submit that based on the publications cited by the Examiner, one skilled in the art would not have been motivated to form a methanesulfonate salt and it could not be predicted whether the methanesulfonate salt necessarily would exhibit a higher melting point and have higher thermal stability than other acid addition salts. Therefore, even if one skilled in the art considers the cited publications, one would not have been motivated to make the methanesulfonate salt of the compound A to arrive at the presently claimed compound and the superior thermal stability of the methanesulfonate compound would not have been expected.

Furthermore, as disclosed at page 5, lines 1-11 of the specification, the thermal stability of the hydrochloride of compound A of Nakai et al. was poor, the crystallinity of the compound was poor and the yield of the crystal thereof was very low.

In contrast, as disclosed at page 11, line 26 to page 12, line 6 of the specification, the presently claimed compound (methanesulfonate) is not only superior in thermal stability but also in solubility and disposition, and the yield of the crystal thereof is very high. Additionally, the presently claimed compound can be supplied stably and is suitable for industrial production, and is superior in forming drug products.

Nakai et al. does not teach or suggest the superior features of the presently claimed methanesulfonate.

Therefore, the present claims are not obvious over Nakai et al.'s claims.

In view of the above, reconsideration and withdrawal of the double patenting rejection based on Nakai et al. are respectfully requested.

At page 3 of the Action, claims 3-6 are objected to as being dependent upon a rejected base claim, but are indicated to be allowable if rewritten in independent form.

Claims 3-6 are patentable in their present form because claim 2, from which claims 3-6 depend, are patentable, as discussed above.

Allowance is respectfully requested. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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